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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |  |  |
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| 10/575,246   | 12/11/2006  | Ge Ming Lui          | P69491US1           | 6963             |  |  |
| 136  | 7590        | 03/25/2008           | EXAMINER            |                  |  |  |
| JACOBSON HOLMAN PLLC<br>400 SEVENTH STREET N.W.<br>SUITE 600<br>WASHINGTON, DC 20004 |             |                      |                     | WANG, CHANG YU   |  |  |
| ART UNIT   |             | PAPER NUMBER         |                     |                  |  |  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                        |                     |  |
|------------------------------|------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b> | <b>Applicant(s)</b> |  |
|                              | 10/575,246             | LUI, GE MING        |  |
|                              | <b>Examiner</b>        | <b>Art Unit</b>     |  |
|                              | Chang-Yu Wang          | 1649                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 18 December 2007.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-25 is/are pending in the application.  
 4a) Of the above claim(s) 1-10 and 18-25 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 11-17 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 4/10/06 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____ .                                    |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/18/06</u> .  | 6) <input type="checkbox"/> Other: _____ .                        |

**DETAILED ACTION**  
***Status of Application/Election/Restrictions***

1. Applicant's election with traverse of Group III (claims 11-17) in the reply filed on December 18, 2007 is acknowledged. The traversal is on the ground(s) that the claims are assumed to be patentable over the prior art and the restriction based on the patentability under PCT rule 13.1 is improper. Applicant also argues that the restriction between Groups I and III is improper because Groups I and III overlap in scope or obvious variants and not capable of being used to make another composition or process as they are limited to corneal epithelial cells. Applicant's arguments have been fully considered but they are not found persuasive. It is noted that the instant application is a 371 national stage application and Applicant's inventions do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features.

MPEP 201 "NATIONAL APPLICATIONS (35 U.S.C. 111) VS. NATIONAL STAGE APPLICATIONS (35 U.S.C. 371)" states that "Treatment of a national application under 35 U.S.C. 111 and a national stage application (a national application which entered the national stage from an international application after compliance with 35 U.S.C. 371) are similar but not identical. Note the following examples: (A) Restriction practice under MPEP § 806 + is applied to national applications under 35 U.S.C. 111(a) while unity of invention practice under MPEP Chapter 1800 is applied to national stage applications".

As previously made of record, Group I was found to have no special technical feature that defined the contribution over the prior art of Klee et al. Adv. Polymer Sci. 2000. 149: 1-57, as in IDS). Thus, Group I cannot share a special technical feature with the other claimed inventions. Accordingly, Applicant's inventions do not contribute a special technical feature when viewed over the prior art, they do not have a single inventive concept and thus lack unity of invention. Although Groups I and III are related

as process of making and product made and may be searched together, they lack unity of invention. In addition, the instant product can be made by a different process, for example obtaining or culturing corneal endothelial cells or epithelial cells as argued by the Applicant from cell lines or live tissues.

Furthermore, as previously made of record (see paragraph 5 in the office action mailed 10/12/07) and reiterated herein, the examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during

prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

In summary, since the 1<sup>st</sup> claimed invention has no special technical feature, it cannot share a special technical feature with the other claimed inventions. Thus, Applicant's inventions do not contribute a special technical feature when viewed over the prior art, they do not have a single inventive concept and so lack unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-25 are pending. Claims 1-10 and 18-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 11-17 are under examination in this office action.

### ***Claim Objections***

3. Claims 1-10 and 18-25 are objected to because of the following informalities: the status of the claims 1-10 and 18-25 are not correct because these claims are withdrawn from consideration. Appropriate correction is required.

See MPEP 714 & 37 CFR 1.121.

"In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered)."

4. Claims 13 and 15 are objected to because of the following informalities: HCEC is not a common abbreviation in the art. Applicants are required to spell out HCEC at the first usage. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11-17 are indefinite because of the term “RGDS” recited in the claims without a reference to a precise amino acid sequence identified by a proper SEQ ID NO: or providing a full name for abbreviated names. Without identification of property or combination of properties which are unique to and, therefore, definitive of the instant recitations, the metes and bounds of the claims remain undetermined. Further, the use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. The rejection can be obviated by amending the claims to specifically and uniquely identify RGDS, for example, by SEQ ID NO. and function of RGDS.

In addition, claims 11-17 are indefinite because the claims recite “approximately”, “average” and “desired”. The terms “approximately”, “average” and “desired” in claims

11 and 13-15 is a relative term which renders the claims indefinite. The terms "approximately", "average" and "desired" are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant fails to set forth the metes and bounds of what is encompassed within the definition of "approximately", "average" and "desired"". Since the metes and bounds cannot be determined, a skilled artisan cannot envision what would be considered as "approximately", "average" and "desired" cornea transplants as recited in the claims.

Thus the claims are indefinite.

#### ***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 11-13 and 17 are rejected under 35 U.S.C. 102 (b) as being anticipated by US Patent No. 5827641 (Parenteau et al. issued on Oct 27, 1998).

Claims 11-13 and 17 are drawn to an artificial full thickness cornea transplant support and an artificial cornea transplant comprising a base biopolymer incorporating an attachment reagent comprising one or more the following: laminin, fibronectin, RGDS, bFGF conjugated with polycarbophil, EGF conjugated with polycarbophil or heparin sulfate, wherein the biopolymer is molded into the shape of a cornea and seeding or not seeding human corneal endothelial cells onto the biopolymer.

US Patent No. 5827641 (the '641 patent) teaches an artificial cornea transplant support and an artificial cornea transplant comprising a biopolymer attached with laminin, fibronectin, RGDS, bFGF or EGF-conjugated with polycarbophil or heparin sulfate as recited in instant claims 11-13 and 17 (see col.5-7, in particular) because the '641 patent teaches an cornea equivalent comprising endothelial cells seeded on membranes made of biopolymer including collagen IV and coated with heparin (i.e.heparin sulfate) and heparin-binding growth factor (i.e.bFGF or EGF-conjugated with polycarbophil). The '641 patent teaches a cornea equivalent (i.e. an artificial cornea transplant) comprising an inner endothelial cell layer, a middle stromal cell-collagen mixture layer and an external epithelial cell layer (see col. 14, claims 1-16; in particular) and use for cornea transplantation. Since the cornea equivalent of the '641 patent encompasses the structures and cell layers of the real cornea and is used for transplantation, the thickness of the cornea equivalent is a full-thickness artificial cornea transplant as recited in instant claims 11 and 13 (see col. 10, lines 1-25, in particular) and the shape is also a desired shape of a cornea as recited in instant claim 11. The '641 patent teaches that the endothelial cells are seeded onto membranes of a cell

culture insert consisting of polystyrene, polycarbonate, polypropylene or collagen (including types I, III-VII and XII), cellulose, glass fiber or other biocompatible polymer, which encompass collagen IV as recited in instant claim 12 and non-swelling biopolymer as recited in instant claim 17 (see col. 5, lines 21-60; col. 6, lines 50-65, in particular). The '641 patent also teaches that the endothelial cells can be derived from different sources including human cornea endothelial cells (see col. 5, lines 1-5; col. 5, line 61-col. 6, line41; col. 8, lines 44-67, in particular). Moreover, The '641 patent teaches different thickness of the cornea equivalent for ocular wound healing, which is not full-thickness (see col. 10, lines 1-25, in particular). Thus, claims 11-13 and 17 are anticipated by US Patent No. 5827641.

### ***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5827641 (Parenteau et al. issued on Oct 27, 1998) in view of US Patent No. 6645715 (Griffith et al. issued on Nov 11, 2003, priority Jan 25, 1999) and US Patent No. 6689165 (issued Feb 10, 2004, priority Mar 31, 2000).

Claims 11-17 are drawn to an artificial full thickness or a half full thickness cornea transplant support and/or an artificial cornea transplant comprising a base biopolymer incorporating an attachment reagent comprising one or more the following: laminin, fibronectin, RGDS, bFGF conjugated with polycarbophil, EGF conjugated with polycarbophil or heparin sulfate, wherein the biopolymer is molded into the shape of a cornea and seeding or not seeding human corneal endothelial cells onto the biopolymer.

US Patent No. 5827641 is as set forth above at paragraph 6 but fails to teach a half full-thickness as recited in instant claims 14-16 and also fails to teach laminin, RGDS, FGF or EGF-conjugated with polycarbophil as recited in instant claims 11 and 14.

US Patent No. 6645715 (the '715 patent) teaches artificial cornea transplant supports or artificial cornea transplants with different thickness comprising a base biopolymer with laminin, fibronectin, RGDS, bFGF conjugated with polycarbophil, EGF conjugated with polycarbophil or heparin sulfate seeding human corneal endothelial cells onto the biopolymer as recited in instant claims 11-17 (see col. 19-24). The '715 patent teaches an artificial mammalian cornea comprising an endothelium, a stromal matrix, an epithelium and at least one layer of Bowman's or Descemet's membrane

(see col. 19-24). The '715 patent teaches that the endothelial cells are grown on collagen coated collagen and mixture with heparin and endothelial cell growth supplement and are seeded onto the membrane of Descemet's membrane, which consists of collagen I and IV mixed with fibronectin and added with polyethylene glycol (PEG) (one of biopolymer) or Bowman's membrane, which consists of collagen I, fibronectin and laminin as recited in instant claims 11-17 (see col. 12, lines 18-55; col. 19-22; col 26, claims 1-22). The '715 patent teaches endothelial cells can be derived from human (see col. 15-16).

US Patent No. 6689165 (the '165 patent) teaches a synthetic device for cornea augmentation or replacement that increases corneal epithelium cell adhesion including extracellular matrix proteins, corneal growth factors and ligand-specific corneal enhancer on the polymeric surface of an artificial cornea such as laminin, fibronectin, integrin, RGDS, FGF, EGF, and TGF-b (see abstract; col. 12-19; col. 19-20, claims 1-18, in particular). The '165 patent teaches that different adhesion attachments allow epithelial cells to proliferate.

It would have been obvious to one of ordinary skill in the art at the time the instant invention was made to modify the artificial cornea transplant/transplant support of the US Patent No. 5827641 to make a different thickness or a half full-thickness artificial cornea transplant or transplant support or to use different attachment agents as recited in the claims. The person of ordinary skill in the art would have been motivated to do so with an expectation of success because different attachment agents have been successfully used to enhance epithelial cell proliferation and some cornea damage does

not require a full-thickness. In addition, the structure of the cornea requires endothelial cells, stromal cells and epithelial cells. The half-thickness cornea transplant/transplant support would allow addition of stromal and epithelial cells of the cornea to the claimed transplant in cornea damage that requires stromal and epithelia cells or to allow proliferation of stromal and epithelial cells to better secure the transplantation.

***Conclusion***

8. NO CLAIM IS ALLOWED.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

US Patent No. 4983181 (issued Jan 8, 1991) teaches that a collagen-hydrogel fixed to Bowman's membrane promotes and supports epithelial cell growth and enables corneal epithelium of an eye.

Insler et al. (p. 139, Cornea. 1991, 10 (2) 136-148, as in IDS) teach transplantation of corneal endothelial cell enhancement or corneal endothelium.

Klee et al. disclosed a method of modifying a biopolymer to enhance endothelial cell attachment and growth comprising coating a polymer with an attachment mixture comprising laminin, fibronectin, RGDS, bFGF and EGF conjugated with polycarbophil (see p. 36-38, 43-53, Klee et al. Adv. Polymer Sci. 2000. 149: 1-57, as in IDS).

10. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with

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the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/

Chang-Yu Wang, Ph.D.

March 6, 2008

/Christine J Saoud/

Primary Examiner, Art Unit 1647